



Managing Lunar and Mars Mission Radiation Risks Part I: Cancer Risks, Uncertainties and Shielding Effectiveness

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GLOSSARY

ALARA	Principle of As Low As Reasonable Achievable
CEV	Crew exploration vehicle
CI	Confidence intervals
CNS	Central nervous system
DDREF	Dose- and dose-rate reduction factor
EAR	Excess additive risk, Sv^{-1}
ELR	Excess lifetime risk (%)
ERR	Excess relative risk, $\text{Sv}^{-1} \text{yr}^{-1}$
F	Fluence, # ions/ cm^2
GCR	Galactic cosmic rays
GSD	Geometric standard deviation
HZE	High charge (Z) and energy (E) ion
HZETRN	High charge and energy transport code
ICRP	International Commission on Radiological Protection
LEO	Low Earth orbit
LET, or L	Linear energy transfer ($\text{keV}/\mu\text{m}$)
LLE	Loss of life expectancy, yr
$M(a)$	Mortality rate to die at age a from all causes of death
$m(E, a, a_E)$	Radiation induced cancer mortality rate to die at age, a after exposure, E at age, a_E
NAS	National Academy of Sciences
NCRP	National Council on Radiation Protection and Measurements
NSRL	NASA Space Radiation Laboratory
PDF	Probability distribution function
$Q(L)$	Quality factor as a function of LET
QMSFRG	Quantum multiple scattering fragmentation
RBE	Relative biological effectiveness
RBE_{max}	Maximum RBE that assumes the dose response is linear at low doses or dose-rates
REID	Risk of exposure induced death (%)
SPE	Solar particle event
x_α	Quantiles (random variables) associated with factor α

Abstract:

We discuss calculations of probability distribution functions (PDF) representing uncertainties in projecting fatal cancer risk from galactic cosmic rays (GCR) and solar particle events (SPE). The PDF's are used in significance tests of the effectiveness of potential radiation shielding approaches. Using Monte-Carlo techniques we propagate uncertainties in risk coefficients determined from epidemiology data, dose and dose-rate reduction factors, quality factors, and physics models of radiation environments to formulate cancer risk PDF's. Competing mortality risks and functional correlations in radiation quality factor uncertainties are treated in the calculations. We show that the cancer risk uncertainty, defined as the ratio of the 95% confidence level (CL) to the point estimate is about 4-fold for lunar and Mars mission risk projections. For short-stay lunar missions (<180 d), SPE's present the most significant risk, however one that is mitigated effectively by shielding, especially for carbon composites structures with high hydrogen content. In contrast, for long duration lunar (>180 d) or Mars missions, GCR risks may exceed radiation risk limits, with 95% CL's exceeding 10% fatal risk for males and females on a Mars mission. For reducing GCR cancer risks, shielding materials are marginally effective because of the penetrating nature of GCR and secondary radiation produced in tissue by relativistic particles. At the present time, polyethylene or carbon composite shielding can not be shown to significantly reduce risk compared to aluminum shielding based on a significance test that accounts for radiobiology uncertainties in GCR risk projection. We conclude that improving knowledge of space radiobiology to narrow uncertainties that lead to wide PDF's is the most effective approach to ensure radiation protection goals are met for space exploration.

1. Introduction

This is the first report in a three part series of reports addressing issues related to managing radiation risks for lunar and Mars missions that will focus on pre-flight safety preparations including risk projections, and shielding effectiveness. The first part addresses cancer risks, the second part acute radiation risks from solar particle events, and the third-part non-cancer risks including damage to the central nervous system. Exposures to astronauts from galactic cosmic rays (GCR), made-up of high-energy protons and high energy and charge (HZE) nuclei, and solar particle events (SPE), comprised largely of low to medium energy protons, are important safety concerns for space exploration. Radiation risks include carcinogenesis, degenerative tissue effects such as cataracts (Cucinotta *et al.*, 2001a) or heart diseases (Preston *et al.*, 2003, Howe *et al.*, 2004, Yang *et al.*, 1982), and acute radiation syndromes (NCRP, 2000). Other risks such as damage to the central nervous system (CNS) are a concern for HZE nuclei (NAS, 1996). In the past, career radiation limits have been based on fatal cancer risks. For low Earth orbit (LEO) programs, an excess fatal risk of 3% is used as criteria for dose limits, which are applied using age and gender specific dose to risk conversion factors. Standards for lunar missions are under review at this time, however it is expected that cancer risks will be the major component of radiation limits until knowledge on chronic non-cancer risks from radiation are more firmly established.

Radiation risk projection models serve several roles, which include setting dose-to-risk conversion factors needed to define dose limits, projecting mission risks, and evaluating the effectiveness of shielding or other countermeasures. For mission planning and operations, NASA uses the model recommended in the NCRP Report No. 132 for estimating cancer risks from space (NCRP, 2000). This model is similar to approaches described by other radiation risk assessment committees or in the scientific literature, employing a life-table formalism, epidemiological assessments of excess risk in exposed cohorts, such as the atomic-bomb survivors, and estimates

of dose and dose-rate reduction factors (DDREF) and linear energy transfer (LET) dependent radiation quality factors. Recently, NASA has recognized that projecting uncertainties in cancer risk estimates along with point estimates should be a requirement for ensuring mission safety, because point estimates alone have limited value when the uncertainties in the factors that enter into risk calculations are large. Estimates of 95% confidence intervals (CI) for various radiation protection scenarios are meaningful additions to the traditional point estimates, and can be used to explore the value of mitigation approaches, and of research that could narrow the various factors that enter into risk calculations. Designing space missions with acceptable levels of cancer risks can take several pathways. Because of the penetrating nature of the GCR, and the buildup of secondary radiation in tissue behind practical amounts of all materials, we have argued previously (Cucinotta *et al.*, 2001b, 2002, 2004) that improving knowledge of biological effects in order to narrow confidence intervals is the most effective approach to achieve radiation safety goals.

Uncertainties for low linear energy transfer (LET) radiation, such as gamma-rays, have been reviewed several times in recent years, and indicate that the major uncertainty is the extrapolation of cancer effects data from high to low doses and dose-rates (NCRP, 1997; BEIR, 1994). Other uncertainties include the transfer of risk across populations, and sources of error in epidemiology data including dosimetry, bias, and statistical limitations. For low LET radiation, probability distribution functions (PDF's) were described previously (NCRP, 1997). In estimating cancer risks for space radiation, additional uncertainties occur related to estimating the biological effectiveness of protons and heavy ions, and predicting LET spectra at tissue sites (Cucinotta *et al.*, 2001b). The limited understanding of heavy ion radiobiology has been estimated to be the largest contributor to the uncertainty for space radiation effects (NAS, 1996), and radiation quality factors were found to contribute the major portion of the uncertainties in a previous study (Cucinotta *et al.*, 2001b).

In this report, we discuss modifications to our methodology for projecting cancer risk probability distributions for space missions, and apply the model to several space exploration mission scenarios including the evaluation of potential shielding approaches: First, in our previous work we had assumed the normal approximation for summing the additive contributions of many radiation components at tissue sites behind spacecraft shielding. The fluence weighted variance for each GCR charge and energy group was summed using the square root of the sum of the squares to estimate the standard deviation and confidence intervals. In the present work, we have used direct sampling over organ weighted LET distributions for the estimation of the 95% CI's, and show that a log-normal distribution results from the analysis. A second modification is related to the uncertainties in the radiation quality factors. Previously, we had considered the range of experimental data for appropriate endpoints in order to develop a subjective PDF for the quality factor. In the present paper, we treat the quality factor, $Q(L)$, and its uncertainties as a functional relationship, which recognizes that values of $Q(L)$ at different LET's are in-fact correlated by underlying biophysical processes. The final improvement made here is to accumulate Monte-Carlo trials directly from the double-detriment life-table rather than the cancer mortality rate. The life-table approach is used because in our previous estimates of cancer risk for the Mars mission (Cucinotta *et al.*, 2001b), the upper level of the 95% C.I. exceeded 10% mortality risk, and for we expect that competing causes of death may significantly compress the higher values in the distribution. By sampling directly from a life-table, we are also able to study a probability distribution for reduced life-expectancy from space radiation exposure. Our risk estimates are based on the quantity, risk of exposure induced death (REID), rather than excess lifetime risk (ELR), in order to properly account for competing risks (Vaeth and Pierce, 1990) and to enable easier comparisons to other space mission risks.

Shielding is one approach that can be considered for mitigating radiation risks. Theoretical and computational efforts in the 1980's and 1990's have provided the basic understanding needed to design effective shielding approaches (Wilson *et al.*, 1991, 1995, Cucinotta *et al.*, 1998a). Materials of low atomic mass, especially hydrogen are expected to be optimal as radiation shields because they reduce the occurrence of secondary particles (neutrons, protons, and other recoils) and are more effective per unit mass of material in slowing down or stopping ions in atomic collisions, and fragmenting HZE ions. However, because relativistic ions in the GCR are not appreciably slowed down by appreciable amounts of any material, and are the largest inducer of secondary radiation produced in tissues, the role of shielding material selection for GCR is not clear. We show here that shielding materials can not be shown to have an important role in reducing GCR risks, because of their poor attenuation properties in any material combined with large risk model uncertainties. In contrast, exposures to SPE's are effectively mitigated by most shielding materials and there is a substantial reduction in mass that occurs when lower mass materials are selected for spacecraft structures.

2. Life-Table Methodology

We use the double detriment life-table to estimate radiation cancer mortality risks. In this approach the age-specific mortality of a population is followed over their entire lifespan with competing risks from radiation and all other causes of death described (Bunger *et al.*, 1981). For a homogeneous population receiving an effective dose E , at age a_E , the probability of dying in the age-interval from a to $a+1$ is described by the background mortality-rate for all causes of death, $M(a)$, and the radiation cancer mortality rate, $m(E, a_E, a)$, as

$$(1) \quad q(E, a_E, a) = \frac{M(a) + m(E, a_E, a)}{1 + \frac{1}{2}[M(a) + m(E, a_E, a)]}$$

The survival probability to live to age, a , following an exposure, E , at age, a_E , is

$$(2) \quad S(E, a_E, a) = \prod_{u=a_E}^{a-1} [1 - q(E, a_E, u)]$$

The excess lifetime risk (ELR) is the increased probability that an exposed individual will die from cancer and is defined by the difference in the conditional survival probabilities for the exposed and unexposed groups as

$$(3) \quad ELR = \sum_{a=a_E}^{\infty} [M(a) + m(E, a_E, a)] S(E, a_E, a) - \sum_{a=a_E}^{\infty} M(a) S(0, a_E, a)$$

We use a finite cut-off of 101-years for the upper limit in Eq.(3) and expressions below. A minimum latency-time of 10-years is often used for low LET radiation (NCRP, 2000), however we will consider alternative assumptions for high-LET radiation. The risk of exposure induced

death (REID) is the lifetime risk that an individual in the population will die from a cancer caused by his or her radiation exposure, defined by

$$(4) \quad REID = \sum_{a=a_E}^{\infty} m(E, a_E, a) S(E, a_E, a)$$

In general, the value of the REID exceeds that of the ELR by about 10-20%. Vaeth and Pierce (1990) have discussed special cases where the ELR is ill-defined and suggested that the REID is the preferred quantity for radiation protection. The loss of life-expectancy amongst exposure induced-deaths, denoted here as LLER, is defined by (Vaeth and Pierce, 1990),

$$(5) \quad LLER = \frac{LLE}{REID}$$

where the average loss of life-expectancy, LLE , in the population is defined by

$$(6) \quad LLE = \sum_{a=a_E}^{\infty} S(0, a_E, a) - \sum_{a=a_E}^{\infty} S(E, a_E, a)$$

2.1 Radiation Carcinogenesis Mortality Rate

For projecting lifetime cancer fatality risks, an age- and gender-dependent mortality rate per unit dose, estimated for acute gamma-ray exposures, is multiplied by the radiation quality factor and reduced by the dose- and dose-rate reduction factor (DDREF) (NCRP, 2000). Additivity of effects of each component in a radiation field is assumed. Radiation mortality rates are largely modeled using the Japanese atomic-bomb survivor data. For transferring risks from the Japanese to US population two models are often considered. The multiplicative transfer model assumes radiation risks are proportional to spontaneous or background cancer risks. The additive transfer model assumes radiation acts independently of other cancer risks. However, the NCRP recommends (NCRP, 2000) a mixture model with fractional contributions from the multiplicative risk model or additive risk model. The radiation mortality rate is written:

$$(7) \quad m(E, a_E, a) = [vERR(a_E, a)M_c(a) + (1-v)EAR(a_E, a)] \frac{\sum_L Q(L)F(L)L}{DDREF}$$

where ERR and EAR are the excess relative risk and excess additive risk per Sievert, respectively, $M_c(a)$ is the gender and age-specific cancer mortality rate in the US population, F is the tissue-weighted fluence, L is the LET, and Q the quality factor. In Eq.(7), v is the fractional division between the assumption of the multiplicative and additive risk transfer models. For solid-cancer, it is assumed that $v=1/2$ and for leukemia that $v=0$.

3. Uncertainties in the Projection Model

Equation (7) consists of a product of several factors: the ERR or EAR , the background cancer rates, M_c , the effective dose represented by the physical dose, FL , times the radiation quality factor, $Q(L)$, and the dose- and dose-rate reduction factor, $DDREF$. The limiting behavior

of the addition of many random variables is well known as the normal distribution. In contrast, the limiting behavior of the multiplication of many random factors will be a log-normal distribution. Equation (7) assumes each multiplicative factor is independent. This assumption may not be strictly valid because of possible correlations between factors or non-additivity of different radiation components, since cells will be traversed by multiple particles and delta-rays produced by ions passing through adjacent cell layers (Cucinotta *et al.*, 1998b). We next consider estimates of the range of values and associated PDF's for each of these factors. Because the risk for longer duration missions exceeds a few percent, upper 95% CIs may exceed 10%. In such cases, the sampling of rates is insufficient and the expression for the REID given by Eq. (4) must be used because of competing risks from other causes of death that will reduce the likelihood of very large radiation risks. Therefore in the sampling approaches described below trials are accumulated for the REID rather than the mortality rate. A criteria used in our approach for formulating PDF's for various factors is ensure the PDF's are peaked at the values recommended by the NCRP (NCRP, 2000), such as the DDREF and Q, or in the current physics models of radiation environments and transport used in mission projections or spacecraft designs. We next discuss the uncertainties in the projection model.

3.1 Uncertainties in Low-LET Epidemiology Data

For sampling purposes, the low-LET mortality-rate per Sievert, m_L is written

$$(8) \quad m_l(E, a_x, a) = \frac{m_0(E, a_x, a)}{DDREF} \frac{x_D x_s x_T x_B}{x_{Dr}}$$

where m_0 is the baseline mortality rate per Sievert (see Eq. (7)) and the x_α are quantiles (random variables) whose values are sampled from an associated probability distribution functions (PDF), $P(x_\alpha)$. Note that the DDREF applies only to the solid cancer risk and not the leukemia risk under the stated assumptions. The NCRP Report 126 (NCRP, 1997) defines the following subjective PDF's, $P(x_\alpha)$, for each factor that contributes to the acute low LET-risk projection:

1. $P_{dosimetry}$ represents the random and systematic errors in the estimation of the doses received by atomic-bomb blast survivors. It is assumed as a normally-distributed PDF for bias correction of random and systematic errors in the dosimetry (DS86) with mean 0.84 and standard deviation 0.11;
2. $P_{statistical}$ represents the distribution in uncertainty in the risk coefficient r_0 . It is assumed as a normally distributed PDF with a mean of one and a standard deviation of 0.15;
3. P_{bias} represents any bias resulting for over- or under-reporting cancer deaths. P_{bias} is assumed as a normal distribution with a most probable values of 1.1 and a 90% C.I. from 1.02 to 1.18 corresponding to a standard deviation of 0.05;
4. $P_{transfer}$ represents the uncertainty in the transfer of cancer risk following radiation exposure from the Japanese population to the US population. Both additive and relative risks models were considered by NCRP 126 in assessing the uncertainties in such transfer. $P_{transfer}$ is log-normal with mean 1 and standard deviation 0.26 (GSD=1.3);
5. P_{Dr} represents the uncertainty in the knowledge of the extrapolation of risks to low dose and dose-rates, embodied in the dose and dose-rate reduction factor (DDREF). The NCRP assumed P_{Dr} to be a truncated triangle distribution starting at 1 and ending at 5 with a peak at 2 with a relative value of $\frac{1}{4}$ or $\frac{1}{2}$ at 1 or 5, respectively, compared to the peak values for the DDREF at 2. This PDF is used to scale the low LET risk coefficient (mortality rates) in our estimates for space radiation.

The NCRP also considered a PDF for bias correction in projection of cancer risks over a lifetime. It is ignored herein because the astronaut population is generally over age 30 and the Japanese data is now complete for these ages. We also ignore the assumed “unknown uncertainties” from the NCRP 126 report (NCRP, 1997).

3.2 Uncertainties due to Dose-Rate and Protraction Effects for Ions

For low dose-rate and protracted proton and HZE radiation exposure of more than a few months, new biological factors may influence risk assessments including redistribution in the cell cycle, repopulation, or promotional effects, especially when particle fluences are large enough to lead to multiple hits of target cells or surrounding cells and tissue environments. Also, not only is there no human data for protons and HZE ions, there is very little experimental data at low dose-rates for these particles. Confidence in using radio-epidemiological data for acute (A-bomb survivors) or fractionated (patients) data is decreased when applied to protracted exposure. Burns *et al.* (1994) found split doses of argon ions separated by a few hours up to one-day increased the risk of skin cancer in rats. Alpen *et al.* (1994) found using seven two-week fractions of 0.07 Gy of iron an increase in risk of 50% compared to a single acute dose of 0.4 Gy for Harderian gland tumors in mice. A study of chromosomal aberrations in human lymphocytes (George *et al.*, 2001) for acute and low dose-rates (0.08 Gy/hr) with 250 MeV protons, showed less sparring than found for gamma-rays. The Skyhook study of Ainsworth *et al.* (1986) considered life-shortening in mice comparing single acute with weekly fractions of several ions, however the results were unclear with regards to any increase or decrease in risk.

For gamma-rays and neutrons, a good number of studies for cancer induction or life-shortening in mice exists, showing sparring effects for gamma-rays, and that neutron effects may be increased due to protraction under certain conditions in some tissues (Ullrich, 1984; NCRP, 1990). Important questions related to the differences in life-span, cell turn-over rates, or mechanisms of initiation or promotion in humans and mice, make estimates of the effects of protraction on risk difficult. If protraction effects do increase the risk from high LET radiation, then such effects would be more important for a Mars mission than the shorter lunar missions. In space, each cell will be traversed about every two to three days by a proton or delta-ray produced by ions in adjacent cells, and with a decreasing frequency from weeks to months as the charge of the HZE nuclei increases (Cucinotta *et al.*, 1998b). Studies of mixed-fields of protons and HZE ions are needed to understand uncertainties in dose-rate and protraction effects from space radiation. Uncertainties related to radiation quality, dose-rate, and protraction could lead to correlations that will be difficult to describe when based on limited experimental data. Methods to treat correlation effects will be needed when data on protraction effects become available.

3.3 Radiation Quality and Latency or Temporal Patterns of Risk

There is an additional radiation quality uncertainty introduced by the scaling assumption used in Eq. (7) because the time dependence for low and high LET radiation is assumed to be identical. Data on tumors or genomic instability in mice with neutrons (Ullrich *et al.*, 1984; 1998; NCRP, 1990) and the studies of rat or mammary carcinogenesis with HZE nuclei (Burns, *et al.*, 1994; Dicello *et al.*, 2004), suggest that the latency time is appreciably reduced for high LET compared to low LET radiation. There is sparse data available to estimate the impact of these differences on uncertainties. A radiation quality dependent latency is more important in the additive transfer model than the multiplicative transfer model, especially at younger ages of

exposure. Also, for high-LET radiation a constant ERR with time after exposure assumption, following an early latency period is difficult to prove based on current animal carcinogenesis data. We ignore these uncertainties; however we replace the 10-year minima latency assumption made for low LET by the step-in latency model (Pierce *et al.*, 1996) used for the leukemia risk. The effects of these assumptions will need to be addressed when data and knowledge on underlying mechanisms become available.

3.4 Uncertainties in Quality Factors

Radiation quality factors represent the largest uncertainty in estimating space radiation cancer risks. Past reviews on the relative biological effectiveness of high-LET radiation include the ICRU Report 40 (1986), NCRP Report 104 (1990), and more recently ICRP Report 92 (2003). The practice of assigning radiation quality factors followed by committees is to consider an average of the relative biological effectiveness (RBE) factors at low doses (RBE_{max}) for the most relevant experimental endpoints. Uncertainties in assignment of RBE's for protons and heavy ions arise for several reasons including sparseness of data for tumorigenesis in animal models or surrogate tissue or cellular endpoints, variability in reference radiation and doses and dose-rates employed, and lack of data over the LET range of interest. Also, linearity at low dose or dose-rates for the reference radiation or ions is often not sufficiently established in experiments. Statistical limitations often hinder studies at the low dose-rates of interest for space radiation protection. For high-LET radiation, a turn-over or bending found in the dose response for tumor induction and neoplastic transformation is observed at moderate doses, presenting further uncertainties in estimating the effectiveness of high-LET radiation at low dose-rates.

Figure 1 shows representative examples of the ratio of RBE_{max} to Q for mouse tumors, cell transformation or mutations, or cytogenetic endpoints. The ratio is often 2- to 3-fold times higher or lower than unity, which indicates the expected deviation from Q in available data. **Table 1** shows LET values at the maximum RBE found in past studies, selected from experiments where >5 ions were employed. Large deviations from the Q peak at 100 keV/ μ m are observed in these experiments with a range from about 50 to 190 keV/ μ m for the peak. These data are largely from the facilities at Berkeley US, Darmstadt Germany, Chiba Japan, and the Alternating Gradient Synchrotron (AGS), Brookhaven National Lab US. The number of past studies and endpoints used are limited if viewed as surrogate endpoints for human carcinogenesis. Additional data for more appropriate endpoints should become available in the next few years at the NASA Space Radiation Laboratory (NSRL). Track structure models suggest that each ion species would have distinct RBE curves of similar shape, however with curves for lower charge ions peaking at a lower LET than higher charged ions (Katz *et al.*, 1971; Cucinotta *et al.*, 1996; Nikjoo *et al.*, 1999). Furthermore, above about 1-MeV/u, lower charged ions have a higher biological effectiveness than higher charged ions of identical LET. Based on track structure models, we expect that data sets that consider only a few ions are insufficient for defining the radiation quality dependence of Q . LET response curves also are predicted to depend on the target size (for e.g. gene or chromosome region), and intrinsic radiation sensitivity, which includes the competition with cell death. These factors likely vary between tissues.

To account for the uncertainties in quality factors, we introduce a trial function that has a shape guided both by experimental data and biophysical models, and sample from distributions of parameters that enter into the functional form. The $Q(L)$ trial function is defined

$$(9) \quad Q_{trial}(L) = \begin{cases} 1 & L < L_0 \\ AL - B & L_0 \leq L < L_m \\ C / L^p & L \geq L_m \end{cases}$$

We sample values of L_0 , L_m , p , and the maximum value, $Q_m(L_m)$ from PDF's described below. Using Eq.(9) we can then solve for values of the constants A, B, and C. Often discussed issues on the definition of $Q(L)$ as embodied in Eq.(9) are the value of slope p that controls the decrease in $Q(L)$ above a maximum, the maximum value of $Q(L)$, the LET where the maximum occurs, L_m , and the minimum LET where $Q(L)$ rises above unity, L_0 . We note the ICRP-60 Q-function corresponds to $L_0=10$ keV/ μ m, $L_m=100$ keV/ μ m, $p = 1/2$, and $Q_m=30$ such that $A=0.32$, $B=2.2$, $C = 300$, and the ICRP-26 Q-function, $L_0=3.5$ keV/ μ m, $L_m=172.5$ keV/ μ m, $p=0$, and $Q_m=20$.

Table 1. Approximate LET where maximum RBE was found in biological experiments.

Biological system	Endpoint	LET at peak RBE, keV/ μ m	LET range (No. of ions studied)	Reference
Human TK6 lymphoblasts cells	TK mutants	60	32-190 (6)	Kronenberg (1994)
Human TK6 lymphoblasts cells	HPRT mutants	60	32-190 (6)	Kronenberg (1994)
Human lung fibroblasts	HPRT mutants	90	20-470 (9)	Cox and Masson (1979)
Human Skin fibroblasts	HPRT mutants	150	25-920 (7)	Tsuoboi <i>et al.</i> (1992)
V79 Chinese hamster cells	HPRT mutants	90	10-2000 (16)	Kiefer <i>et al.</i> (1994); Belli <i>et al.</i> (1993)
<i>Caenorhabditis elegans</i>	Recessive lethal mutations	190	0.55-1110 (14)	Nelson <i>et al.</i> (1989)
Human lymphocyte cells	Chromosomal exchanges	147	0.4-1000 (10)	George <i>et al.</i> (2003)
Human fibroblast cells	Chromatid breaks	80-185	13-440 (6)	Kawata <i>et al.</i> (2001)
C3H10T1/2 mouse cells	Transformation	140	10-2000 (10)	Yang <i>et al.</i> (1989)
C3H10T1/2 mouse cells	Transformation	90	20-200 (10)	Miller <i>et al.</i> (1995)
Syrian hamster embryo (SHE) cells	Transformation	90	20-200 (8)	Martin <i>et al.</i> (1995)
Mouse (B6CF ₁)	H. gland tumors	185*	2-650 (6)	Fry <i>et al.</i> (1985)
Mouse (B6CF ₁)	H. gland Tumors	193	0.4-1000 (7)	Alpen <i>et al.</i> (1993)
Mouse (CB6F ₁)	Days life lost	52*	50-500 (6)	Ainsworth (1986)

*Track-segment or spread-out Bragg peak (SOBP) irradiations.

The parameter samplings are based on the following assumptions for PDF's:

- a) L_0 : equal probability between 5 and 10 keV/ μm , and decreasing to zero at 1 keV/ μm , or above 15 keV/ μm .
- b) L_m : equal probability for LET values between 75 and 150 keV/ μm , and decreases to zero at 50 keV/ μm or above 250 keV/ μm .
- c) p : equal probability between $p=1/2$ and 1, and decreasing to zero at $p<0$ or $p>2$.
- d) Q_m : log-normal distribution with mean value of 30 and GSD of 1.8.

Figure 2 shows examples of trial $Q(L)$ functions that contribute in the sampling procedures, and **Figure 3** shows the resulting average $Q(L)$ and 95% CI after 20,000 trials. The resulting range is smaller than in our previous report (Cucinotta *et al.*, 2001b), however should be a reasonable estimate when the effects of dose protraction are not included in the uncertainty analysis.

3.5 Uncertainties in Physics: Environments and Transport Codes

Space dosimetry and radiation transport codes have been studied extensively in the past, and although there are no major scientific questions that lead to errors in the assessment of space radiation environments, there are uncertainties due to limitations in dosimetry flown on past space missions. For application of computational models, the level of detail that has been used in transport code comparisons is often limited, with common simplifications the use of an aluminum equivalent shielding approximation, simplified geometries, and no description of orientation effects. Approaches to assess the errors in space dosimetry include inter-comparison of different dosimetry on the same missions, and to results of space radiation transport models. Statistical errors in the assessment of physical doses are quite small (<5%), however inter-comparisons between laboratories have shown differences on the order of 10% for absorbed dose (Badhwar, 1997). Comparisons of transport calculations to measurements of LET spectra or dose equivalent should consider response functions of different detector types to charged particles or neutrons (Nikjoo *et al.*, 2002). Commonly used detectors are tissue equivalent proportional counters (TEPC's), silicon detectors, and CR-39 plastic track detectors. However, good agreement has been found in the limited number of comparisons that have been made (see for e.g., Badhwar and Cucinotta, 2000; Kim *et al.*, 2003; Shinn *et al.*, 1998), especially when detector response functions are represented in the comparisons.

Models of the GCR environment rely on the large number of spaceflight and balloon measurements that have been made, and apply the diffusion theory of Parker (1965) to describe the modulation of the GCR over the solar cycle. The root mean square error for GCR environmental models is less than 10% for the major GCR elements and less than 15% for most minor elements (Badhwar and O'Neill, 1994a; Badhwar *et al.*, 1994b; O'Neill, 2005). The isotopic composition of the GCR is also represented in transport codes (Cucinotta *et al.*, 2003) used in risk calculations. Solar particle event spectra vary from event to event, and there is no method available to predict the fluence, energy spectra, or dose-rates of a future event. In the present report we discuss calculations for the large SPE of August of 1972. Risk assessment approaches to SPE's for acute risks will be considered in a future report. Transport codes rely on data bases for nuclear interaction cross sections including inclusive single differential in energy or total fragment production cross sections for projectile fragments, and double differential in energy and angle for lighter mass secondaries (neutrons, hydrogen and helium ions, and mesons). Cross-section data are sparse for some projection-target combinations and in the number of energies, especially above 1,000 MeV/u. Three dimensional aspects of transport from angular scattering, a small correction for high-energy ions, are expected to be an important correction for neutrons and other light mass ions. Computer codes that use multi-group methods or Monte-Carlo

simulations to describe angular effects on neutron transport have been developed for GCR shielding applications. The Monte-Carlo codes are limited by the computational times needed to describe spacecraft with thousands of parts, and the multi-group methods by the ability to describe complex geometries. However, because flight measurements and the results of the HZETRN code (Wilson *et al.*, 1995) using the Badhwar-O’Neill GCR input spectra (Badhwar and O’Neill, 1994), and QMSFRG nuclear interaction data base (Cucinotta *et al.*, 2003) are in good agreement, it is unclear if such developments will have an important impact on risk assessment.

Differences between transport models and flight dosimetry that account for the detectors response to different radiation components are generally small with absolute differences within 10% for the GCR dose, and 20% for the GCR dose equivalent (Badhwar, 1997; Badhwar and Cucinotta, 2001; Cucinotta *et al.*; 2000; Cucinotta *et al.*, 2003). Measurements of dose or dose-equivalent may not provide sufficient information on possible errors in predicting LET spectra because compensating errors can occur. Also, neutron spectra are difficult to assess within complicated spacecraft and tissue geometries. In particular, measurements or calculations of neutron spectra are expected to lead uncertainties in LET spectra in the LET range from about 30 to 300 keV/μm where recoil nuclei deposit the majority of the energy. Neutrons also cause a low LET gamma-ray component often ignored in calculations. Larger errors are expected at higher LET where stopping nuclei dominate and may be difficult to define due to local tissue variations. We expect uncertainties to be larger at high LET values where the role of local target recoils, and stopping GCR primaries are difficult to describe.

The PDF’s for the uncertainties in LET spectra, should ensure the resulting dose equivalent is consistent with transport code comparisons to past spaceflight measurements for GCR. A quantile, x_L , associated with a normal distribution, $P_F(x_F=F/F_0)$ is used with a standard error that increases with LET to represent the higher uncertainties expected for prediction of neutron effects, and difficulty in precisely defining stopping ions in complex geometries. The PDF is given a median of $x_{OF}=0.65$ to ensure the resulting dose equivalent is in agreement with values from prior comparison between transport codes and flight measurements cited above. Standard deviations for different LET regions are given in **Table 2**.

Table 2. Standard deviations for uncertainties in model LET spectra for several LET regions.

<i>LET Interval</i>	<i>S.D. for dF/dL</i>
< 30 keV/μm	1.0
30-300 keV/μm	2.0
> 300 keV/μm	2.5

Figure 4 and **Figure 5** illustrate the errors assigned to environmental and physical factors in evaluating LET spectra at tissue sites.

3.6 Life-Tables and Population Cancer Rates

Radiation risk calculations are based on population data, however are used to estimate risks for individuals. Population data reflect gender differences, however also change with calendar year and often used for projections far into the future. For the astronaut population, the appropriateness of using the US average population can be questioned, because the so-called “healthy worker” effect is expected for astronauts. In the average US population, females have

longer life span than males, partially due to overall lower risk of cancer. The formalism of Eq.'s (1)-(7) show two counter-acting effects arise when one attempts to determine if the use of population rates representative of a healthier population compared to the US population would decrease or increase the risk of radiation carcinogenesis. First, the population survival function acts to decrease radiation risks, especially at older ages. Therefore an improved survival function acting alone will increase the risk from radiation. However, an improved survival function also suggests lower background cancer rates, making up some fraction of the delay in mortality. In the multiplicative transfer model, radiation risks are reduced if a healthy worker effect is due in-part to reduced natural incidence of cancer. Thus, the portions of the risk transfer assigned to multiplicative and additive transfer act in opposition if a healthy worker effect is present. In a model where a geometric average of these two models is used, we expect a minor change if an improved life-table and background cancer rates are assumed. The role of the survival function is also reduced if solid cancers would display a plateau at long times after exposure (>30 yrs), as has been suggested in some studies (Preston *et al.*, 2003). This discussion points to the need for better understanding of the biological basis for risk transfer models, and dependence of risk after long follow-up times.

In order to estimate the effects of gender and calendar year specific population data on radiation risk projections, **Table 3** shows results for males and females receiving an exposure of 1 Sv were radiation rates are fixed, but life-tables and/or cancer rates for females and males, respectively are varied between the genders. It can be seen that these changes lead to variations of no more than $\pm 20\%$. The higher cancer risk for females is thus largely due to the additional risks for breast and ovarian cancer, with lifespan differences between genders making a minor contribution. The Social Security Administration (SSA, 2004) has looked at projections of life-expectancy over the next 75-years, which spans the period of the Mars exploration program. Their results given in **Figure 6**, show about a 6-year increase in life-expectancy for males and females over this time period. Since in the year 2000 life-tables, females have about a 6-yr higher life expectancy than males, the examples shown in **Table 3** for males using the female population rates also serve to illustrate the change expected due to calendar-year evolution of population rates over the course of the next 75 years. The differences between males and females also suggest the level of change that could occur if healthy worker population rates were modeled. The comparison indicates changes on the order of 10% over the next few decades; however larger changes would occur using a purely multiplicative transfer model.

Table 3a. Sensitivity study of REID(%) for males at 1 Sv effective dose estimated using male radiation rates and female life-table and population cancer rates. Percent changes from altering these background rates are listed in parenthesis.

Age, yr	Males	Males with female M(a), M _c (a)	Males with female M(a)	Males with female M _c (a)
30	4.84	5.20 (+7.4)	5.99 (+23.8)	4.23 (-12.6)
40	3.76	4.08 (+8.5)	4.63 (+23.1)	3.33 (-11.4)
50	2.59	2.83 (+9.3)	3.21 (+23.9)	2.29 (-11.6)

Table 3b. Same as 3a for Females.

Age, yr	Females	Females with male M(a), M _c (a)	Females with male M(a)	Females with male M _c (a)
30	6.45	6.24 (-3.3)	5.20 (-19.4)	7.79 (+20.8)
40	4.83	4.63 (-4.1)	3.91 (-19.1)	5.77 (+19.5)
50	3.27	3.13 (-4.3)	2.62 (-19.9)	3.92 (+19.9)

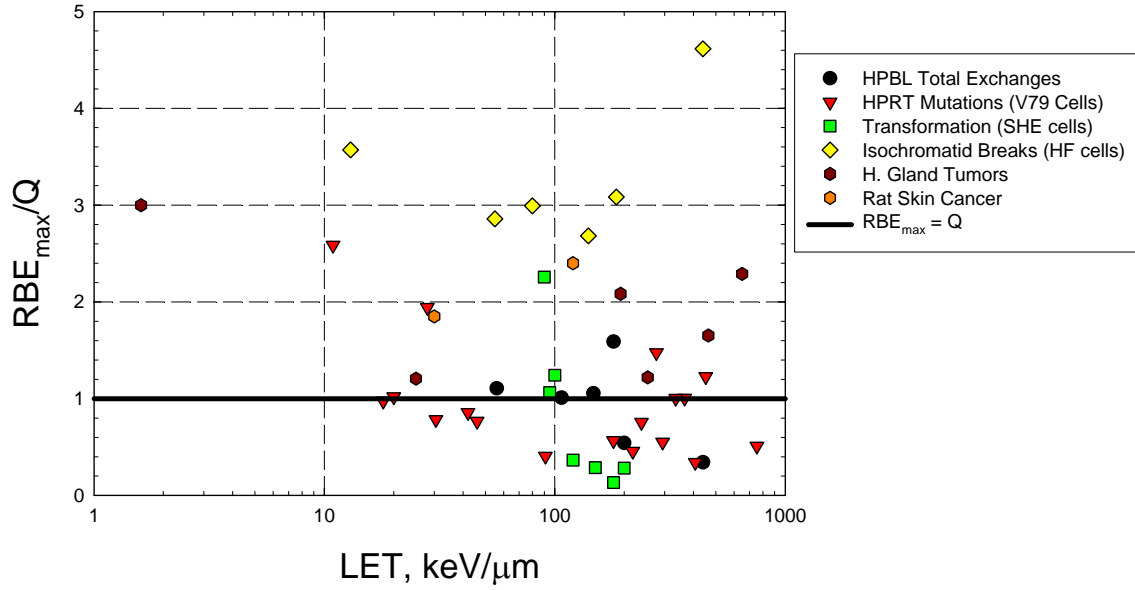


Figure 1. Comparison of ratio of RBE_{max} to Q for several endpoints found with proton, alpha particle, and heavy ion irradiations (Reference to experiments listed in Table I).

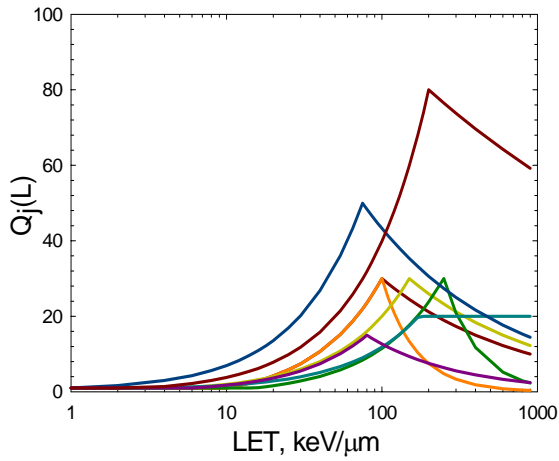


Figure 2. Examples of trial quality factor functions used in uncertainty calculations. A distinct curve is generated for each trial.

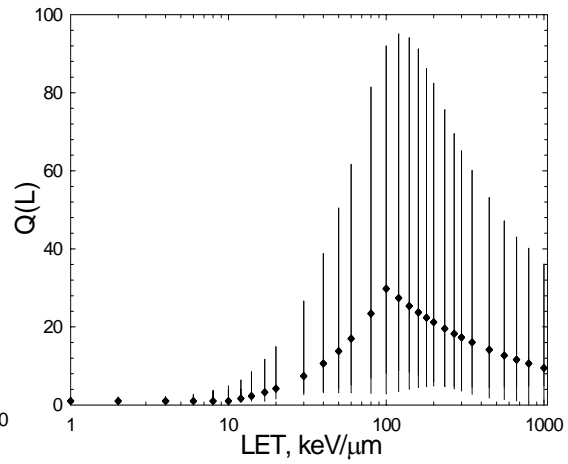


Figure 3. Average quality factor (circles) and 95% CI's versus LET that from Monte-Carlo sampling over trial function of Eq. (9).

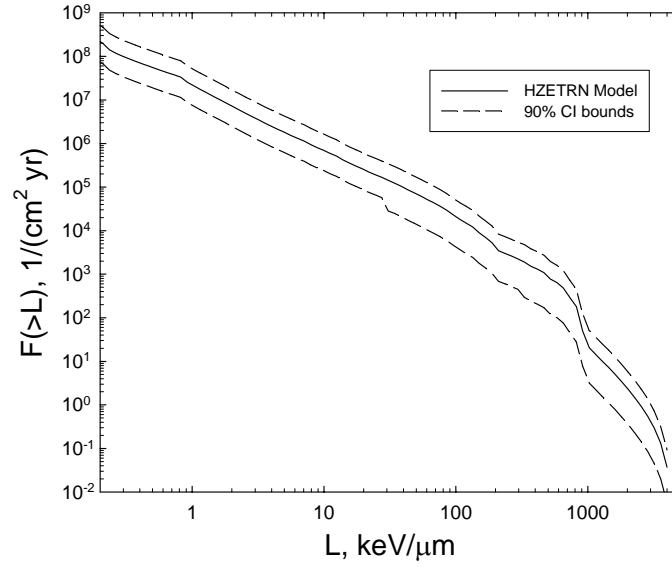


Figure 4. Calculation of tissue weighted integral LET spectra and 90% CI for space environmental and transport uncertainties for 20 g/cm² aluminum shield for 1-year in deep space.

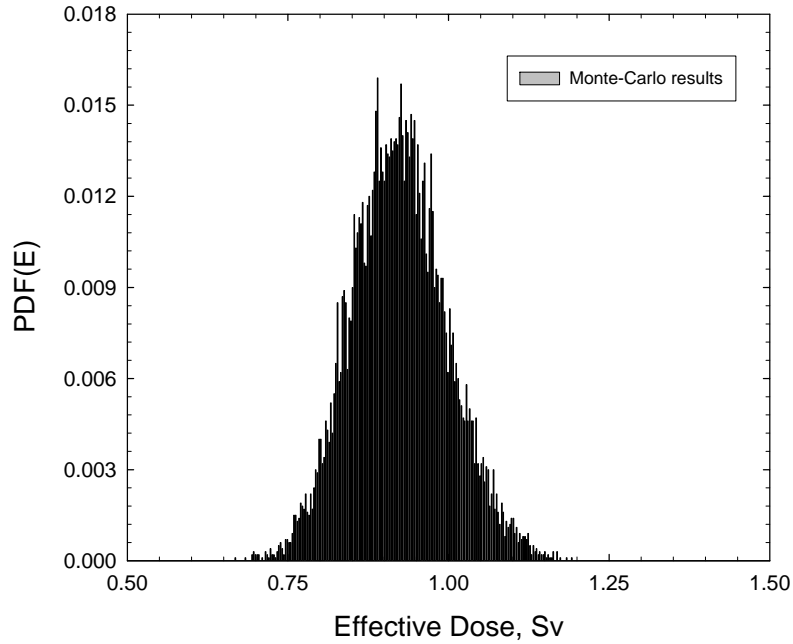


Figure 5. PDF for GCR effective dose for 20 g/cm² aluminum shield for 600-d Mars swing-by mission. The point estimate is 0.86 Sv, and the 95% CI for uncertainties in LET distribution at tissue sites is [0.78, 1.08] Sv. Only uncertainties in physics are included.

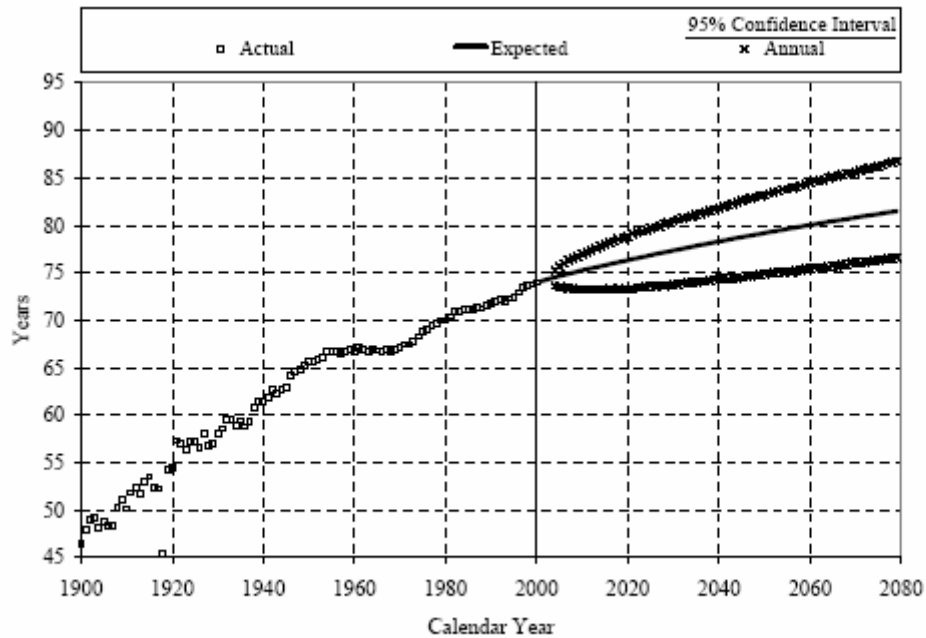


Figure 6a. Actual or projected male median lifespan at birth versus calendar year (from Social Security Administration, 2004).

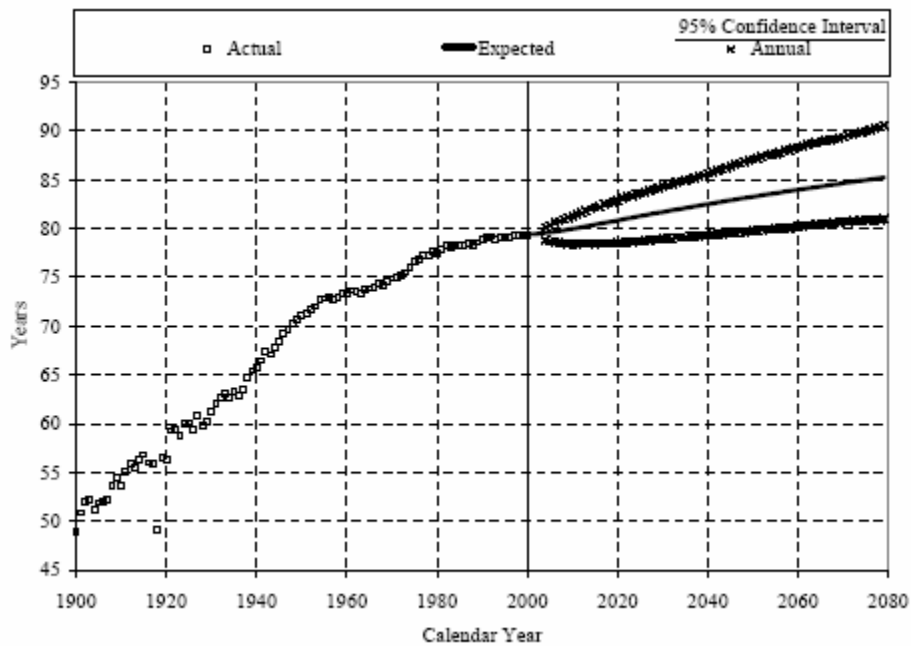


Figure 6b. Actual or projected female median lifespan at birth versus calendar year (from Social Security Administration, 2004).

4. PDF's for Space Exploration Missions

The cancer risk projection for space missions are found by folding predictions of the tissue-weighted LET spectra behind space craft shielding, dF/dL , with the radiation cancer mortality rate to form a rate for a trial J :

$$(10) \quad m_j(E, a_E, a) = m_{ij}(E, a_E, a) \int dL \frac{dF}{dL} L Q_{trial-J}(L) x_{L-J}$$

(not shown are quantiles associated with low-LET mortality rate). Alternatively, particle specific energy spectra, $F_j(E)$ for each ion, j , can be used:

$$(11) \quad m_j(E, a_E, a) = m_{ij}(E, a_E, a) \sum_j \int dE F_j(E) L(E) Q_{trial-J}(L(E)) x_{L-J}$$

The result of equation (10) or (11) is then inserted into the expression for the REID of equation (4). In implementing a numerical procedure, we group the PDF's related to the risk coefficient of the normal form, which consist of the dosimetry, bias, and statistical uncertainties into a combined PDF, $P_{cmb}(x)$. After accumulating sufficient trials ($\sim 10^5$), the results for the REID estimates are binned and the median values and confidence intervals found.

We use the χ^2 test for determining if PDF's for two distinct shielding configurations or materials are significantly different. We denote the calculated PDF's for a REID of R_i for two configurations or materials as $p_1(R_i)$ and $p_2(R_i)$, respectively. Each $p(R_i)$ follows a Poisson distribution with variance, $\sqrt{p(R_i)}$. The chi-squared, χ^2 test for characterizing the dispersion between the two distributions is then,

$$(12) \quad \chi^2 = \sum_n \frac{[p_1(R_n) - p_2(R_n)]^2}{\sqrt{p_1^2(R_n) + p_2^2(R_n)}}$$

Once χ^2 is determined, the probability $P(n, \chi^2)$ that the two distributions are the same is calculated. If χ^2 is sufficiently large such that $P(n, \chi^2)$ is less than about 20%, is an indication that we can conclude that the two distributions lead to distinct cancer risks from GCR and/or SPE's, with the material with the lowest mean and upper 95% CL values preferred for radiation protection. However, the opposite result indicates that the either the materials are approximately the same, or that the uncertainties in risk models prevents us from concluding that either configuration or material is superior for radiation protection properties. We evaluate χ^2 for the LET dependent parts of the uncertainties (quality factors and physics) separately, since only these contributions explicitly depend on the modification of radiation fields by shielding.

5. Results

In the results described next we use values of *ERR* and *EAR* for solid cancers from the Japanese Longitudinal Lifespan Study Report No. 13 (Preston *et al.*, 2003). Note that these values for females were found to about 15% lower than the prior Report No. 12 (Pierce *et al.*, 1996) used by NCRP Report No. 132 (NCRP, 2000) and values for males nearly the same in Reports 12 and

13. Values for *ERR* and *EAR* for leukemia were not updated in the latest report and we use the values from Pierce *et al.* (1996). We use life-tables (CDC, 2000) and background cancer mortality rates (SEER, 2000) for the average US population for the year 2000. For models we use the GCR free space environment of Badhwar *et al.* (1994b), the HZETRN transport code (Wilson *et al.*, 1991, 1995), and the QMSFRG model of nuclear fragmentation cross-sections (Cucinotta *et al.*, 2003). The CAMERA model (Billings and Yucker, 1973) is used for organ shielding with tissue weighting coefficients (NCRP, 2000). **Figure 7** shows calculations of the point dose equivalent and the effective dose (tissue averaged organ dose equivalent) for various shielding materials calculated by the HZETRN/BRYNTRN codes for the solar minimum GCR environment and the August of 1972 SPE. Calculations predict that the effects of SPE are readily mitigated by shielding, the effects of GCR are not, and tissue shielding reduces the differences expected when comparing materials. For hydrogen shielding, the GCR effective dose is larger than the point dose because target fragments in tissue contribute about 50% of the effective dose, even though very little secondary radiation is produced directly in the hydrogen shield. Clearly, calculations or measurements of point dose equivalents mis-represent the effectiveness of shielding because of the role of secondary radiation produced in tissue.

Spacecraft typically have aluminum as a major constituent and transport calculations often scale material thicknesses under an aluminum equivalent areal-density $t=\rho x$, approximation where ρ is mass density and x , physical thickness, and materials are scaled to aluminum by the ratio of the range of 60 MeV protons or a similar approximation. **Figure 8a** shows the Apollo command module and a recent Crew Exploration Vehicle concept (CEV) and **Figure 8b** thickness distributions in aluminum equivalent depths for several spacecraft. Minimal areal-densities of spacecraft such as the Skylab, the Space shuttle or International Space Station are 2 to 5 g/cm²; however averages are in the range from 10-25 g/cm² of aluminum equivalent material. Many dose calculations in the scientific literature under-estimate the inherent shielding of spacecraft and tissues. For calculations, we use 5, 10, and 20 g/cm² as representative of minimal or average shields. Complex shielding configurations are a superposition of these results (Cucinotta *et al.*, 2000); however transition effects between materials should be considered.

Figure 9 shows calculations for the point estimate and 95% CI's for risk versus LET for males exposed at age 40 y. The top panel shows risks at an absorbed dose of 0.01 Gy and the bottom panel at 0.1 Gy. The solid squares are the resulting "fold-uncertainty" defined as the ratio of the 95% CL to the point estimate. At high LET, a 5-fold uncertainty occurs at low absorbed dose, however at higher absorbed dose and near the peak LET effectiveness, the uncertainties are reduced to about 3-fold due to competing causes of death limiting the upper levels of risk from radiation. **Figure 10** shows the REID dose response for iron ions (1000 MeV/u) and illustrates how curvature arises due to competing risks.

NASA is considering various lunar and Mars missions as part of the exploration vision. A spiral concept is planned where Spirals 1, 2, and 3 are missions to the moon, and Spirals 4 and 5 are Mars swing-by and surface missions, respectively. Approximate characteristics of these missions used in our calculations are described in **Table 4**. The variation of GCR and SPE over the solar cycle would be difficult to use as a trade variable in long-term planning and we therefore discuss calculations at solar minimum and near solar maximum. We consider cancer risk calculations for Spirals 3-5. For solar maximum calculations, we assume the large solar particle event (SPE) of August, 1972 to occur during the inter-planetary part of the mission, and use a solar modulation parameter (Badhwar *et al.*, 1994) of 1100 MV, typical of about two years past solar maximum, however when large SPE's often occur. SPE worst-case risks will be considered in part II of this series of reports. Note that SPE exposures on the lunar surface are reduced by approximately one-half by the moon itself, and on the Mars surface by more than one-half due to

the planet and the Mars atmosphere. We use a 16 g/cm² vertical height for the Mars CO₂ atmosphere in our calculations.

Table 5 shows fatal cancer risk projections at solar minimum for males and females of age 40 at the time of the mission. Cancer morbidity risks are about 50% higher than mortality risks described here. Calculations are made for minimally shielded spacecraft of 5 g/cm² aluminum, and a heavily shielded one of 20 g/cm². Similar calculations near solar maximum are shown in **Table 6** with an SPE fluence equivalent to the August of 1972 SPE is assumed to have occurred. At solar minimum, it is seen that a four-fold addition of mass reduces the cancer risk by only about 15%. Results are different at solar maximum. Here a four-fold increase in shielding mass leads to more than two-fold reduction in cancer risk; solar protons are less penetrating than GCR and effectively mitigated by shielding. However for heavy shielding (≥ 20 g/cm²), GCR dominates over SPE's and further addition of shielding provides marginal reductions. Each SPE is unique and has distinct fluence and energy spectra, and dose rates, therefore the shielding thickness where GCR doses exceed SPE doses vary from event to event.

Table 4. Summary of mission parameters used for NASA spiral mission risk estimates.

<i>Spiral</i>	<i>Time period</i>	<i>Total Days</i>	<i>Deep Space Days</i>	<i>Lunar or Mars surface Days</i>
1 (Lunar)	2015-2020	6	6 (LEO)	0
2	2018-2025	14	6	8
3	2020-2030	90	6	84
4 (Mars)	2030-2040	600	600	0
5	2030-2040	1000	400	600

An alternative to a shielding approach that adds mass is to optimize materials used in spacecraft structures or planetary habitats to reduce radiation risk. **Figure 11** shows PDF's for the GCR as solar minimum for aluminum, polyethylene, and liquid hydrogen shielding with areal density of 20 g/cm². **Table 7** shows results for the χ^2 statistic comparing polyethylene and hydrogen shielding effectiveness to aluminum. For calculations that ignore the low LET risk coefficient uncertainties, near solar maximum with a large SPE, significant results ($P < 0.01$) are found for liquid hydrogen, and for the GCR at solar minimum (with $P < 0.15$). We conclude that because of the modest differences between polyethylene and aluminum as GCR absorbers, and the large radiobiological uncertainties in cancer risk projection models, the benefits of polyethylene compared to aluminum shielding for GCR can not be proven at this time. A key factor in these results is that although aluminum is a greater producer of secondary radiation compared to polyethylene, tissue shielding "equalizes" much of these differences.

The formalism can be applied to estimate the number of days a mission is ensured to be below an exposure limit at a given confidence level. Because we use the REID quantity, and the newer LSS Report 13 (Preston *et al.*, 2003) values for ELR and EAR compared to the NCRP Report 132 (NCRP, 2000), and consider limits for single missions rather than 10-year careers, we first calculated dose limits that result for the present model corresponding to 3% and 5% fatal cancer risk for missions of length < 3 yr. These are listed in **Table 8**, which also shows calculations of loss of life-expectancy (LLE) from radiation cancer induced cancers. In an earlier report (Cucinotta, *et al.* 2000b) we estimated the maximum number of days in deep space astronauts could spend with a 95% CL to remain below a 3% fatal cancer risk. **Table 9** updates these calculations and compares to the earlier report. The results show a significant increase in the number of "safe" days with 95% CL to remain below acceptable levels or risk that result from our improved methodology. However, the results are well short of that needed for a Mars mission.

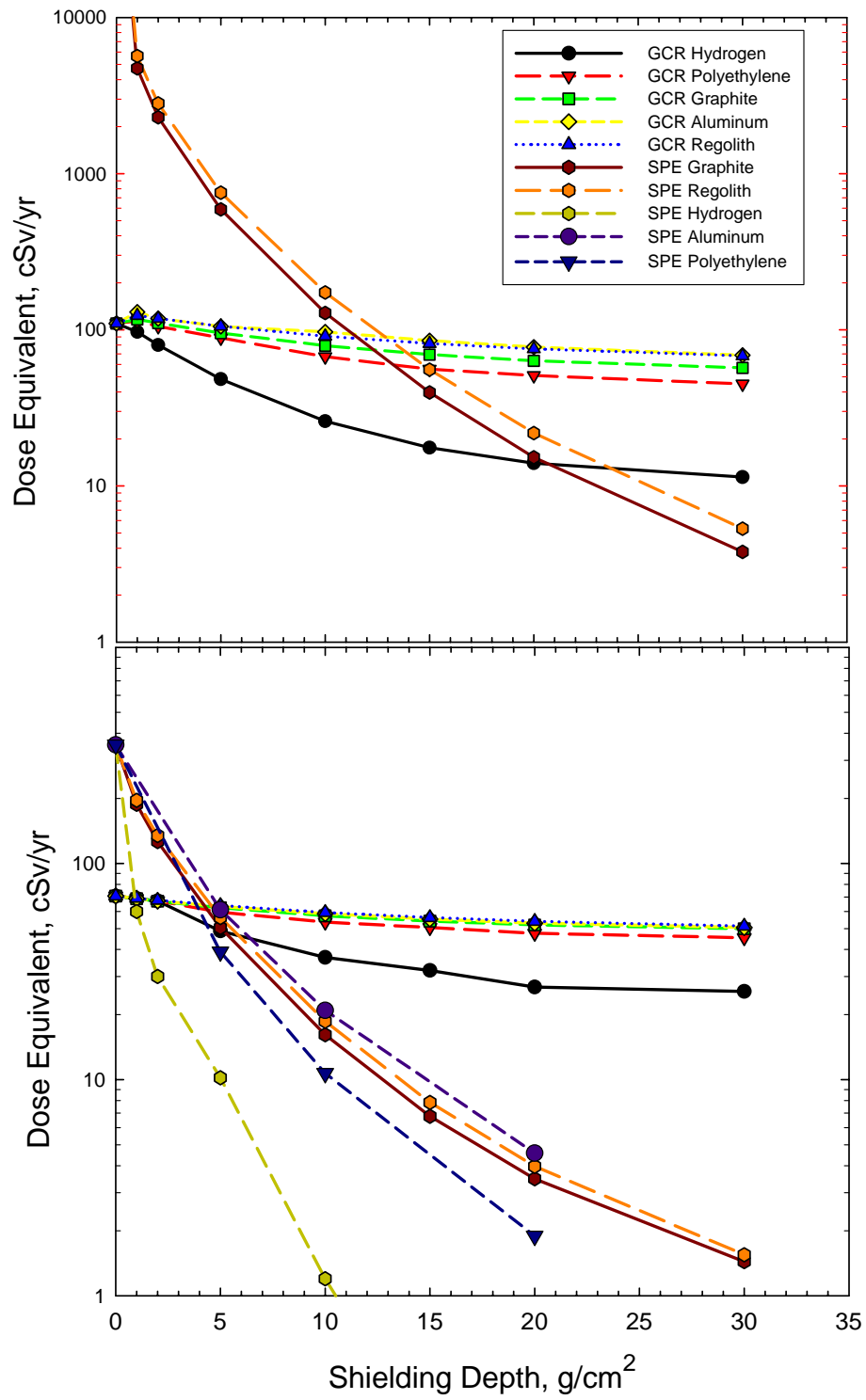


Figure 7. Point dose equivalent (upper panel) and effective dose (bottom panel) behind various shields for solar minimum GCR and August 1972 SPE (the units for the SPE doses are for total event and not necessarily per year).

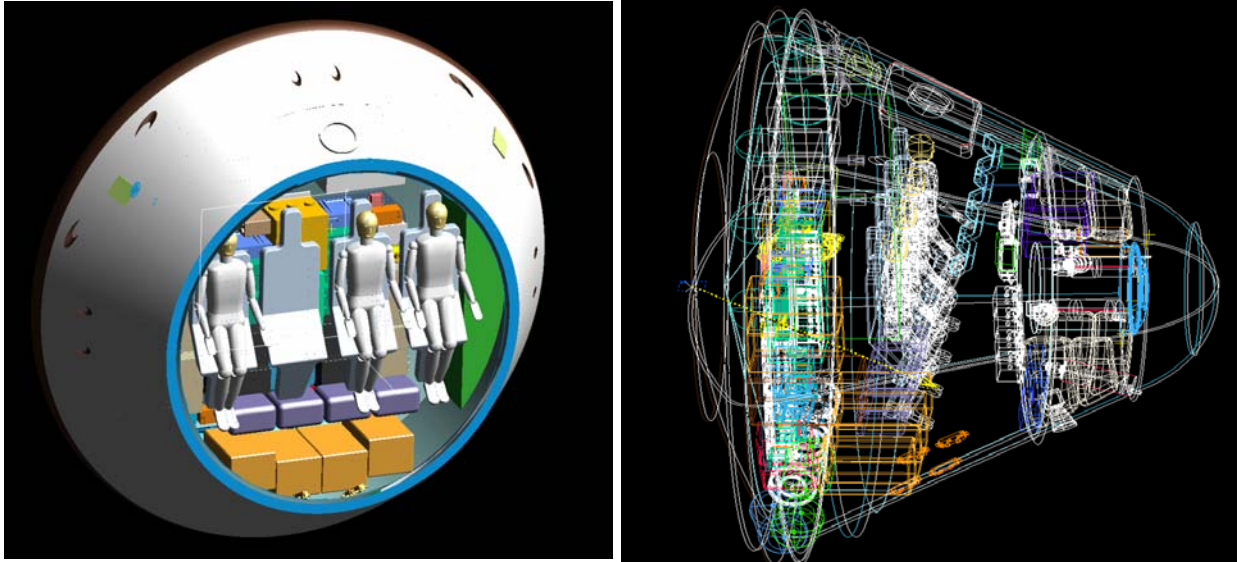


Figure 8a. Computerized aided design (CAD) model of JSC Exploration Division C.E.V. concept. Green area in left panel shows polyethylene shield added to design to increase protection from SPE's (J. Lenius, T. Cooper, M. Shavers, and F.A. Cucinotta, unpublished).

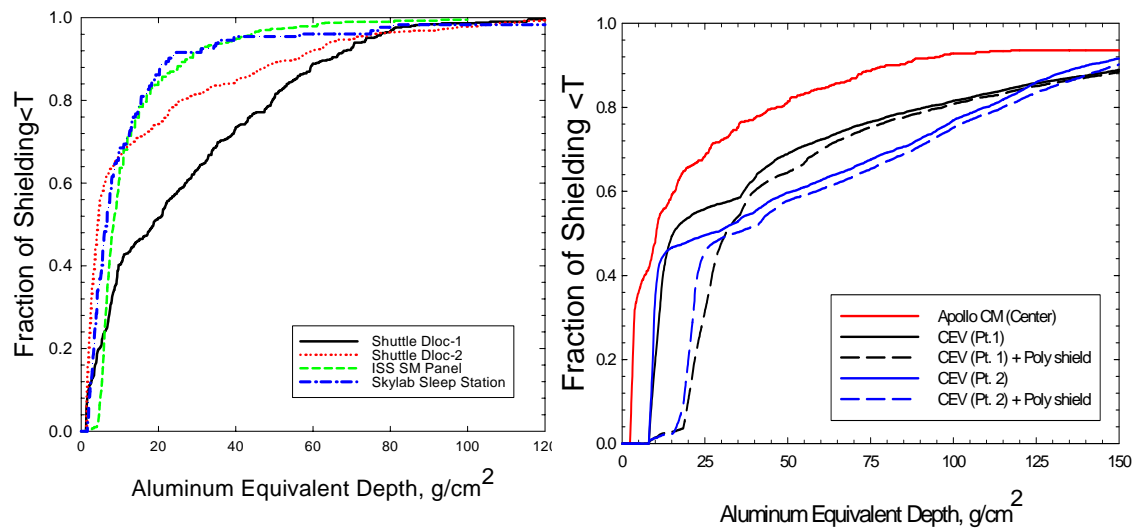


Figure 8b. Mass distributions in aluminum equivalent depths: Left panel in Space shuttle, ISS Service Module, and Skylab commander sleep compartment, and Right Panel for Apollo command module and two points in CEV model with and without storm shelter addition.

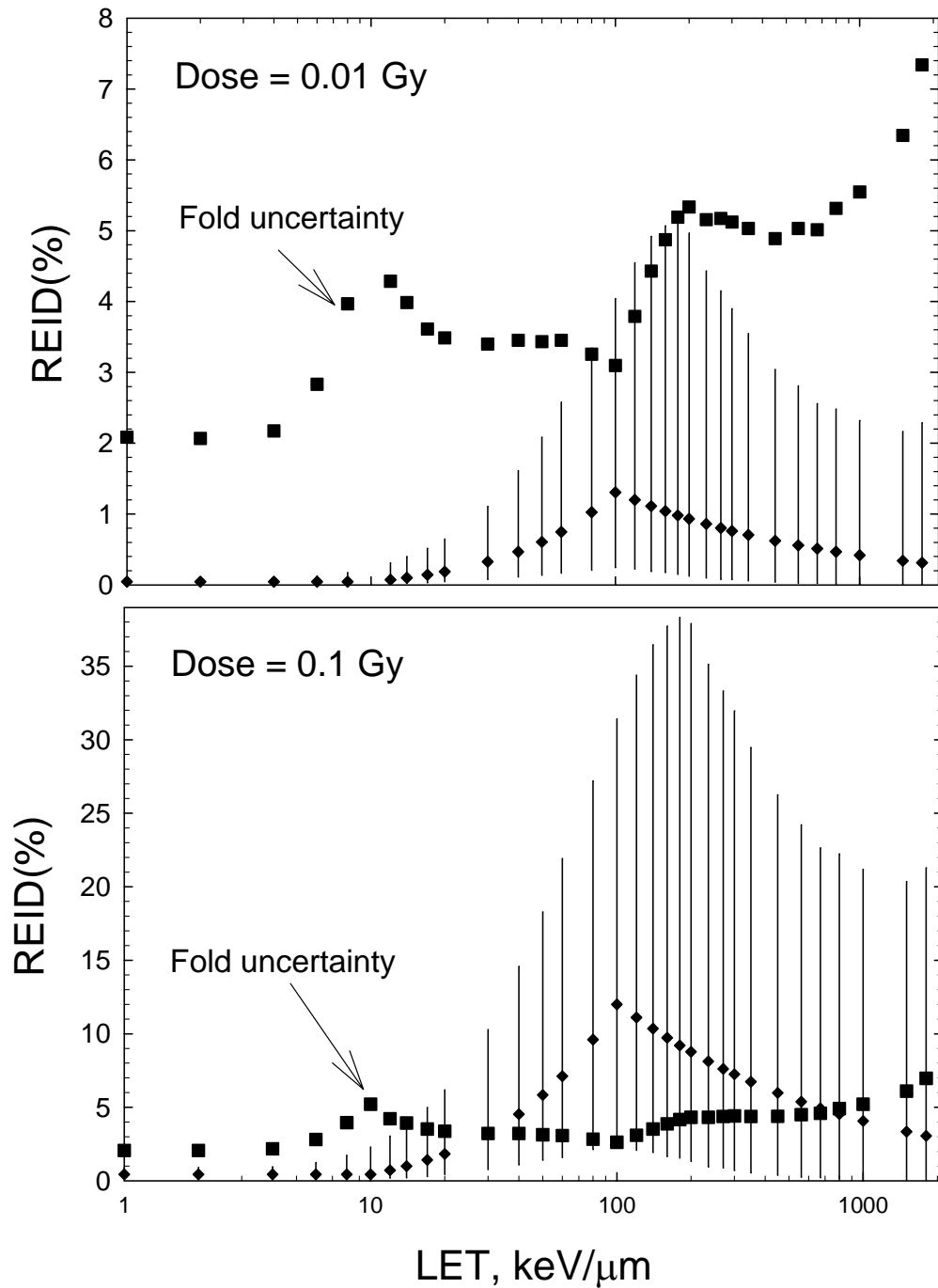


Figure 9. Calculations of REID versus LET at doses of 0.01 or 0.1 Gy for 40-y males. Diamonds point estimates, bands 95% CI, and squares the fold uncertainties.

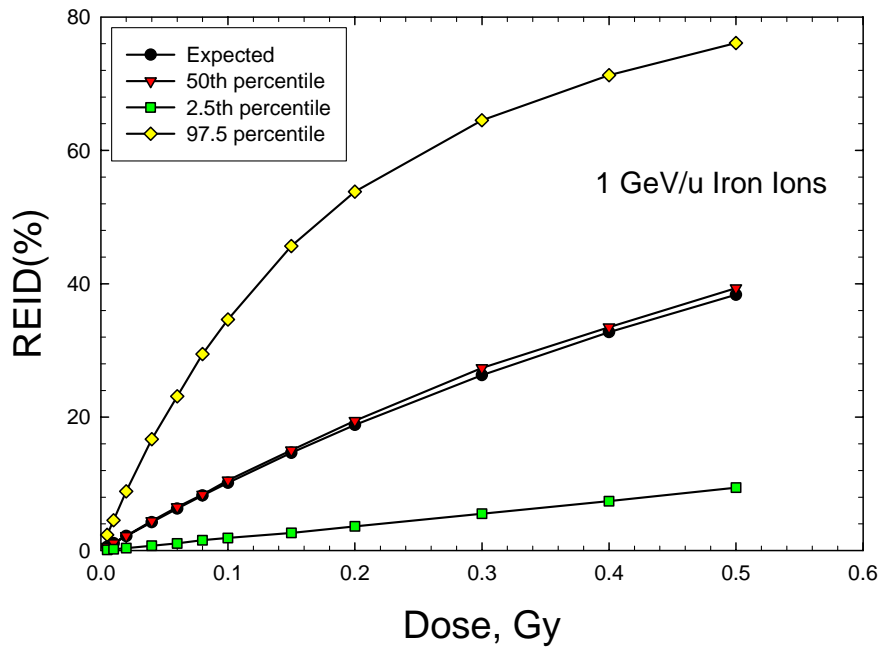


Figure 10. Dose response for point estimate and confidence levels for 1 GeV/u iron ions showing curvature in the response at high risk levels due to competing risks.

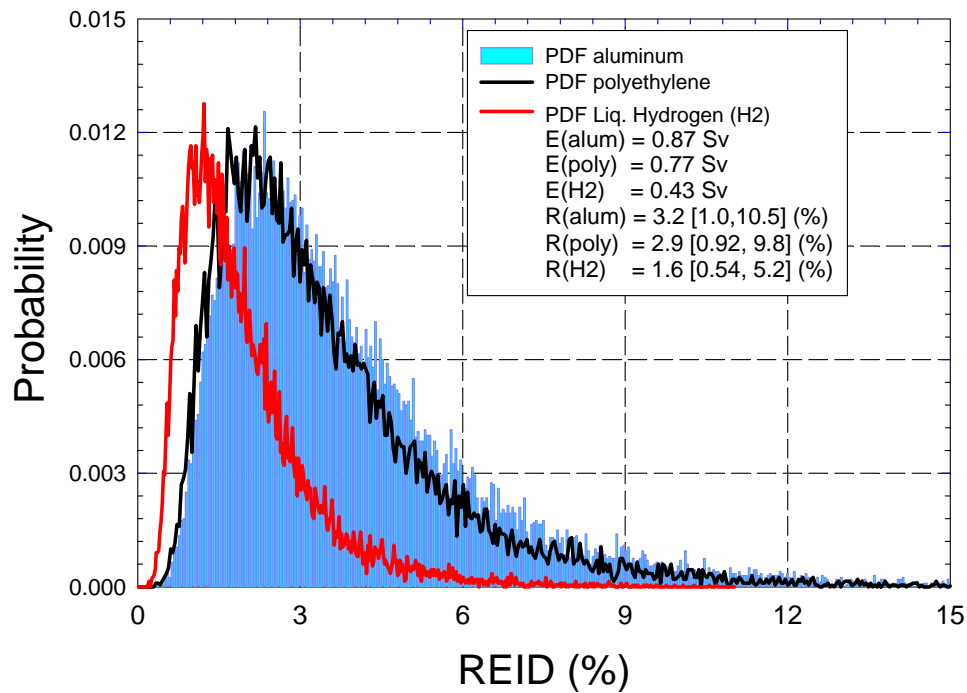


Figure 11. PDF's for 40-y males on Spiral 4 for 20 g/cm² shields of aluminum, polyethylene or liquid hydrogen. Effective doses, and point estimates and 95% CI for REID are shown in box.

Table 5a. Calculations of Effective doses, REID, and 95% CI for lunar or Mars missions. Calculations are at solar minimum for a 5 g/cm² aluminum shield.

<u>Spiral</u>	<u>D, Gy</u>	<u>E, Sv</u>	<u>REID(%)</u>	<u>95% CI</u>
Males (40 y)				
3	0.03	0.084	0.34	[0.10, 1.2]
4	0.37	1.03	4.0	[1.0, 10.5]
5	0.42	1.07	4.2	[1.3, 13.6]
Females (40 y)				
3	0.03	0.084	0.41	[0.12, 1.5]
4	0.37	1.03	4.9	[1.4, 16.2]
5	0.42	1.07	5.1	[1.6, 16.4]

Table 5b. Calculations of Effective doses, REID, and 95% CI for lunar or Mars missions. Calculations are at solar minimum for 20 g/cm² aluminum shield.

<u>Spiral</u>	<u>D, Gy</u>	<u>E, Sv</u>	<u>REID(%)</u>	<u>95% CI</u>
Males (40 y)				
3	0.03	0.071	0.28	[0.09, 0.95]
4	0.36	0.87	3.2	[1.0, 10.4]
5	0.41	0.96	3.4	[1.1, 10.8]
Females (40 y)				
3	0.03	0.071	0.34	[0.11, 1.2]
4	0.36	0.87	3.9	[1.2, 12.7]
5	0.41	0.96	4.1	[1.3, 13.3]

Table 6a. Calculations of Effective doses, REID, and 95% CI for lunar or Mars missions. Calculations are near solar maximum assuming 1972 SPE in deep-space segment of mission with 5 g/cm² aluminum shield.

<u>Spiral</u>	<u>D, Gy</u>	<u>E, Sv</u>	<u>REID(%)</u>	<u>95% CI</u>
Males (40 y)				
3	0.45	0.69	2.7	[0.95, 7.6]
4	0.62	1.21	4.4	[1.5, 13.1]
5	0.66	1.24	4.8	[1.6, 14.2]
Females (40 y)				
3	0.45	0.69	3.3	[1.1, 9.3]
4	0.62	1.21	5.7	[1.8, 17.1]
5	0.66	1.24	5.8	[2.0, 17.3]

Table 6b. Calculations of Effective doses, REID, and 95% CI for lunar or Mars missions. Calculations are near solar maximum assuming 1972 SPE in deep space segment of mission with 20 g/cm² aluminum shield.

<u>Spiral</u>	<u>D, Gy</u>	<u>E, Sv</u>	<u>REID(%)</u>	<u>95% CI</u>
Males (40 y)				
3	0.04	0.09	0.36	[0.12, 1.2]
4	0.22	0.54	2.0	[0.60, 6.8]
5	0.25	0.60	2.4	[0.76, 7.8]
Females (40 y)				
3	0.04	0.09	0.43	[0.13, 1.4]
4	0.22	0.54	2.5	[0.76, 8.3]
5	0.25	0.60	2.9	[0.89, 9.5]

Table 7a. χ^2 test at solar minimum for 20 g/cm² shields for 40-yr males on Mars swing-by mission. $P(n, \chi^2)$ is the probability materials can not be determined to be significantly different (n=500). Values in bold for $P(n, \chi^2) < 0.2$ indicate a significant improvement over aluminum.

Test Material	E, Sv	REID(%)	95% CL	χ^2/n	$P(n, \chi^2)$
All Uncertainties					
Aluminum	0.87	3.2	[1.0, 10.5]	-	-
Polyethylene	0.78	2.9	[0.94, 9.2]	0.05	>0.99
Hydrogen	0.43	1.6	[0.52, 5.1]	0.63	>0.99
LET-dependent Uncertainties					
Aluminum	0.87	3.2	[1.9, 8.7]	-	-
Polyethylene	0.78	2.9	[1.8, 7.5]	0.08	>0.99
Hydrogen	0.43	1.7	[1.0, 4.2]	1.10	<0.15

Table 7b. Same as **Table 7a** near solar maximum for 5 g/cm² shields.

Test Material	E, Sv	REID(%)	95% CL	χ^2/n	$P(n, \chi^2)$
All Uncertainties					
Aluminum	1.21	4.4	[1.5, 13.1]	-	-
Polyethylene	0.94	3.5	[1.2, 10.8]	0.14	>0.99
Hydrogen	0.52	2.1	[0.60, 6.4]	0.81	>0.99
LET-dependent Uncertainties					
Aluminum	1.21	4.4	[3.0, 11.0]	-	-
Polyethylene	0.94	3.5	[2.3, 8.8]	0.32	>0.99
Hydrogen	0.52	2.1	[1.2, 5.2]	1.38	<0.001

Table 7c. Same as **Table 7a** near solar maximum for 20 g/cm² shields.

Test Material	E, Sv	REID(%)	95% CL	χ^2/n	$P(n, \chi^2)$
All Uncertainties					
Aluminum	0.54	2.0	[0.60, 6.8]	-	-
Polyethylene	0.45	1.7	[0.52, 5.6]	0.08	>0.99
Hydrogen	0.24	0.9	[0.27, 2.9]	0.77	>0.99
LET-dependent Uncertainties					
Aluminum	0.54	2.0	[1.2, 5.6]	-	-
Polyethylene	0.45	1.7	[1.0, 4.6]	0.15	>0.99
Hydrogen	0.24	0.9	[0.52, 2.4]	1.26	<0.005

Table 8a. Example career effective dose limits in units of Sievert (Sv) for 1-year missions and corresponding average life-loss for an exposure induced death.

	E, Sv for 3% REID (Ave. Life Loss per Death, yr)	
Age, yr	Males	Females
25	0.5 (15.7)	0.4 (15.9)
30	0.6 (15.4)	0.5 (15.7)
35	0.7 (15.0)	0.55 (15.3)
40	0.8 (14.2)	0.6 (14.7)
45	0.95 (13.5)	0.75 (14.0)
50	1.15 (12.5)	0.9 (13.2)
55	1.5 (11.5)	1.1 (12.2)

Table 8b. Example career effective dose limits in units of Sievert (Sv) for 1-year missions and corresponding average life-loss for an exposure induced death.

	E, Sv for 5% REID (Ave. Life Loss per Death, yr)	
Age, yr	Males	Females
25	0.9 (15.7)	0.6 (15.9)
30	1.0 (15.4)	0.8 (15.7)
35	1.2 (15.0)	0.9 (15.3)
40	1.3 (14.2)	1.0 (14.7)
45	1.6 (13.5)	1.25 (14.0)
50	1.9 (12.5)	1.5 (13.2)
55	2.45 (11.5)	1.9 (12.2)

Table 9a. Projections for males of age-dependent maximum days in deep space with 95% CL of remaining below a risk limit, R_L (%). Calculations are for GCR at solar minimum with 10 g/cm² aluminum shielding comparing previous results (Cucinotta *et al.*, 2001b) to present results.

Age, yr	Previous $R_L=3\%$	Present $R_L= 3\%$	Present $R_L= 5\%$
30	91	142	236
35	104	166	277
40	122	186	310
45	148	224	373
50	191	273	455
55	268	340	568

Table 9b. Projections for females of age-dependent maximum days in deep space with 95% CL of remaining below a risk limit, R_L (%). Calculations are for GCR at solar minimum with 10 g/cm² aluminum shielding comparing previous results (Cucinotta *et al.*, 2001b) to present results.

Age, yr	Previous $R_L=3\%$	Present $R_L= 3\%$	Present $R_L= 5\%$
30	54	112	187
35	62	132	220
40	73	150	250
45	89	182	304
50	115	224	374
55	159	282	470

6. Discussion and Recommendations

The building of PDF's that propagate errors from individual factors that contribute to uncertainties in projection models is a powerful tool for managing radiation risks, including evaluating benefits of research and mitigation approaches and implementing the radiation protection principle of as low as reasonable achievable (ALARA). The uncertainties estimated here are reduced compared to our previous estimates (Cucinotta *et al.*, 2001b, 2002, 2004) for the following reasons:

1. Use of the REID rather than radiation cancer rates (decreases upper uncertainty level because of role of competing risks)
2. Use of trial $Q(L)$ functions rather than uncorrelated uncertainties as a function of LET (overall decrease in uncertainties)
3. Neglect of NCRP "unknown" uncertainties (decrease in uncertainties)
4. Re-defining LET-spectra uncertainties (modest increase in uncertainties).

However, these estimates should be viewed as preliminary because of the need to assess additional uncertainties that have not been included in the analysis, including protraction effects, scaling of ERR's or EAR's estimated from low LET data to high LET's, and the potential impact of a healthy worker effect. These factors will need to be considered in future work. Research at NSRL will have a major impact on reducing uncertainties by establishing basic understanding for extrapolating experimental data to humans, and providing important data for reducing the major uncertainties described above (dose-rate effects and quality factors). Low-LET epidemiology data and physics models uncertainties have a smaller role in the present evaluation. As noted in our earlier report (Cucinotta *et al.*, 2001b), other uncertainties exist in the representation of radiation shielding composition and predicting future solar cycle effects or the characteristics of SPE's; however these are more practical in nature and will be considered elsewhere.

The methodologies used for risk assessment ultimately play a large role in the estimates of uncertainties and shielding effectiveness. The use of the linear-additivity model is a key assumption in the current methodology. This model has a strong basis in mouse carcinogenesis studies with low dose neutron irradiations (Storer and Fry, 1995), and for neutron exposures, a mixed low and high-LET field is present due to the gamma-ray component produced by neutrons. However, this would not be representative of the spectral and temporal patterns of GCR. Possible deviations from the linear-additivity model for the GCR spectrum along with correlations in estimates of DDREF, protraction effects and quality factors need to be considered in future work. Experiments that simulate the constant high-energy proton background with interspersed heavy nuclei irradiation such as iron would be a first-step in testing these effects. The NCRP model (NCRP, 2000) applies a DDREF of two only for total doses less than 200 mGy or dose-rates less than 0.1 mGy/min. The former condition is not met for the Mars missions or for a large SPE, and should be investigated in future work. Further investigation of alternative methodologies that could possibly reduce uncertainty estimates should also be considered. The use of Bayesian statistics combined with track structure models to explore the replacement of $Q(L)$ functions with Q functions dependent on charge and LET or kinetic energy, and the resulting effects on uncertainties will be described in a future report. Alternative methodologies including ones that study cancer incidence at specific tissue sites, should allow additional biological factors to enter risk models perhaps lowering uncertainty estimates. However, the need for new biological data and understanding is the most important approach to reducing uncertainties.

Career radiation limits and shielding requirements could also be impacted by new knowledge of fatal non-cancer risks from radiation exposure such as heart disease (Preston *et al.*, 2003; Howe *et al.*, 2004; Yang *et al.*, 1982) or damage to the central nervous system (CNS).

Based on the Japanese survivor data (Preston *et al.*, 2003), non-cancer risks are estimated to be small for the shorter lunar missions, but could lead to a significant risk for the Mars mission. The risk of heart disease for ions is largely unknown because only one report (considered a pilot study by the authors of the report) has been made on the effects of HZE ions on heart disease (Yang *et al.*, 1982), and human data for low LET radiation at low dose-rates is inconclusive on the level of risk to be expected (Howe *et al.*, 2004; Cardis *et al.*, 1995). CNS risks have the potential to impact both short-term and career radiation limits and mitigation approaches (NRC, 1996), however it will be several years before radiobiological research will provide sufficient knowledge on CNS risks to be used operationally by NASA.

As new experimental data and models of cancer risks are obtained from NSRL, we expect a significant reduction in estimates of uncertainties compared to those estimated in the present report. However, there are limitations on the extent of uncertainty reduction that can be achieved by using population based estimates. In the future, the need for performing individual based risk assessment will grow if uncertainties less than about two-fold are to be achieved. A major conclusion of this report is that funding of ground-based space radiobiology research to reduce the uncertainties in risk projections, remains the most cost-effective approach for achieving goals in radiation safety, including ensuring risk mitigation approaches are validated.

We have shown that with regard to the GCR, the optimization of material selection and mass can not be put on a sound scientific basis because the reductions estimated from point estimates alone are only on the order of a 10-30% for most shielding materials, and when combined with the uncertainties in projection models non-significant results for risk reduction are found. It still may be reasonable to assume that risk is reduced when comparing hydro-carbon shields to aluminum or other metals, however application of ALARA is problematic since cost-benefit analysis can not be properly performed under these conditions. In contrast, for acute risks, which are largely an absorbed dose and dose-rate effect, SPE's are the major concern and the role of minimizing mass requirements through hydro-carbon shielding materials is easier to prove. We recommend the following approach for radiation shielding designs until uncertainties are reduced to a degree that significance testing of shielding effectiveness can be based on PDF's:

- 1.) Exploration vehicles should be designed to reduce acute radiation risks from SPE's to well below a 30 day limit of 0.25 Gy-Eq using a worst-case SPE environment that will be discussed in Part II of this report.
- 2.) Secondary to SPE shielding should be the optimization of GCR shielding. A reduction of the following three quantities by more than 25% compared to aluminum should be considered to demonstrate sufficient value in alternative shielding materials:
 - a) Effective dose (organ averaged)
 - b) HZE fluence, $F(E)$ for ions with $Z > 10$
 - c) $F(L)$ for $L > 30 \text{ keV}/\mu\text{m}$
 - d) Neutron fluence, $F(E)$ between 0.1 to 20 MeV.

The requirements in a) through d) are partially redundant, however are needed to ensure that the radiation components with the highest biological uncertainties are significantly reduced when evaluating GCR shielding concepts. Reductions of less than 25% could be considered if the costs for their implementation are low.

The ALARA principle is an important aspect of radiation safety. Our estimate of 95% CL's to stay below limits can be used as criteria for a minimal ALARA requirement for the design of lunar missions including transfer vehicle or surface habitat designs. For example about a 4-fold margin can be used for GCR exposures and about a 2.5 fold margin for SPE's. Detailed cost-benefit analysis should be used for measures that would provide even lower risks. Future work should consider a worst-case SPE environment including the possibility of multiple SPE's

as a function of mission duration. Based on the results of **Table 9** and the above margins, we conclude that “blind selection” of astronauts for lunar missions can be made for missions with duration less than 180 days for male or female astronauts above the age of 35-yrs, if sufficient protection against SPE’s is provided. Because of the higher GCR risks for Spiral 4 and 5, and the likely impacts of non-cancer risks, no conclusions on ALARA goals for these missions or the possibility of “blind selection” can be made at this time. The inherent uncertainties in population based risk models and the higher risks for Spiral 4 and 5 missions; point to the likelihood that individual based risk assessments will be needed for Mars exploration missions.

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